

Materials and methods: 110 pregnant rats were used in this study: untreated (control) rats (n=42), rats orally treated with nebivolol (8 mg/kg/day, n=43), or bisoprolol (10 mg/kg/day, n=25) from day 11 to day 18 of gestation. The systolic blood pressure (SBP) and genital blood flow (GBF) were measured by tail cuff method and transonic method respectively (on the 19th day and 20th of the gestation). In addition, a morphometric study was performed on the ovarian and uterine arteries; fetal weight and postnatal development of three infants randomly chosen are following for 8 weeks. The results are expressed as mean \pm SEM of n experiments.

Results: The results clearly showed that SBP and GBF are lower in rats treated with nebivolol (SBP=115.56 \pm 0.62 mmHg. GBF= 0.20 \pm 0.04 ml/s) compared to untreated rats (SBP=140.14 \pm 0.33 mmHg. GBF=0.53 \pm 0.03 ml/s) or to that treated with bisoprolol (SBP=122.42 \pm 0.28. GBF=0.40 \pm 0.03). The treatment with nebivolol also caused a strong increase of lengths and diameters of the ovarian and uterine arteries. In addition, it increases the number of segmental branches of the uterine artery compared to the other two groups. Moreover, the results showed that nebivolol has an adverse impact on fetal growth and postnatal development. It was found that average weight of a fetus at the end of gestation was (3.55 \pm 0.03 g) with nebivolol, (5.64 \pm 0.01 g) with bisoprolol and (6.05 \pm 0.02 g) in control.

Conclusion: We showed that the action of nebivolol is not only limited to its favorable hemodynamic effects, but nebivolol also produces adverse effects on fetal growth and postnatal development, that may limit its therapeutic use during pregnancy. As wistar female rats were normotensive, we need to further investigate the effect of nebivolol in a hypertensive model.

0247

Changes in blood pressure and arterial mechanical properties after antiangiogenic drugs: association with cancer progression and mortality

Maureen Alivon (1), Julie Giroux (2), Marie Briet (3), François Goldwasser (2), Stéphane Laurent (1), Pierre Boutouyrie (1)
(1) Inserm U970 – PARCC, Service de pharmacologie, Paris, France – (2) Hôpital Cochin-APHP, Oncologie, Paris, France – (3) HEGP-APHP, Centre d'investigations clinique, Paris, France

Objective: Hypertension is a frequent side effect of antiangiogenic drugs (AAD). Targeting VEGF pathway may also affect large and small artery properties, along with or independently of blood pressure changes. We hypothesized that large and small artery property changes in response to AAD reflect their effect on the microcirculation at the site of the tumor, and thus may be related to cancer progression and mortality.

Design and method: We included 60 patients [age 58 (15) years, mean SBP 127(21) mmHg] in whom treatment with AAD was indicated for various metastatic solid tumors. Noninvasive arterial investigation was performed before AAD (V0), 1 week later (V1) and then every two weeks for two months (V1 to V4): carotid-femoral pulse wave velocity (cfPWV), central SBP and augmentation index (cAIx) by applanation tonometry (SphygmoCor®), and carotid stiffness (CStiff) and internal diameter (CiD) by high resolution echotracking (Artlab®). Cancer progression and mortality were assessed at 6 months.



Results and conclusion: 28(47%) patients developed hypertension during follow-up. bSBP significantly increased during follow-up (V0-V1: +9.3 \pm 15.2mmHg, P<0.001; V0-V4: +6.0 \pm 17.8mmHg, P=0.03), as well as PWV, CStiff, and CiD. Baseline cAIx predicted cancer progression (RR=0.73 per 10%) and mortality (RR=0.73 per 10%, P<0.001) while SBP did not. The V0-V1 increase in CStiff predicted cancer progression (RR=1.37 per 1 m/s, P=0.02), independently of age and MBP. In conclusion, increased AIx and arterial stiffness, but not brachial or central SBP, were related with the effects of AAD on cancer progression and mortality.

0350

Renal denervation in resistant hypertension: is it really effective?

Mihaela Cordeanu (1), Eric Prinz (2), Francois Bronner (1), Christine Jahn (3), Sebastien Gaertner (1), Olivier Morel (4), Thierry Hannedouche (2), Dominique Stephan (1)

(1) NHC, Hypertension et Maladies Vasculaires, Strasbourg, France – (2) NHC, Néphrologie, Strasbourg, France – (3) NHC, Radiologie, Strasbourg, France – (4) NHC, Cardiologie, Strasbourg, France

Introduction: Renal denervation is an endovascular technique of sympathetic afferences ablation, currently indicated in resistant hypertension.

Objective: According to the European guidelines, it should be part of a comprehensive therapeutic approach and the object of a multidisciplinary decision. To this purpose, we evaluated our professional practices by analyzing our one-year program of screening for eligible patients.

Patients and Method: Between Oct 2012 and Oct 2013, 10 interdisciplinary reunions including vascular doctors, nephrologists, radiologists and cardiologists took place at the University Hospital of Strasbourg, reviewing 41 cases of resistant hypertension.

Results: The characteristics of the 41 patients were the following: a mean age of 62 \pm 9 years old (mean \pm SEM), predominantly male (66%), a glomerular filtration rate of 67 \pm 23 ml/min/1.73 m² and an ambulatory blood pressure (ABPM) daytime mean of 152/83mmHg \pm 15/14 while receiving 4 \pm 1 antihypertensive drugs daily. Among them, 9 were controlled after adjustment of medical treatment, 5 had a renal artery stenosis, 4 had a fibromuscular dysplasia; there were 2 severe renal impairments and 11 other morphologic exclusion criteria. The 10 patients who finally benefitted from renal denervation had an initial daytime ABPM of 164/93 \pm 11/11 mmHg and an initial office blood pressure of 174/94 \pm 18/23mmHg while receiving 5.2 \pm 0.6 antihypertensive drugs. The follow up visits showed a mean reduction in the office blood pressure of 11.5mmHg \pm 18 at 1 month (n = 9), of 10.5mmHg \pm 10 at 3 months (n = 7) and 14mmHg \pm 25 at 6 months(n = 5).

Conclusion: Renal denervation is an invasive procedure claiming to become part of the armamentarium of antihypertensive treatments, requiring trained operators and prior careful evaluation in order to eliminate remediable causes of treatment resistance. Our preliminary results are mitigated showing a stable and significant resp